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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte NING WEI and RAMESHBABU BOGA

Appeal 2010-005244
Application 10/718,997
Technology Center 1600

Before LORA M. GREEN, MELANIE L. McCOLLUM, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a flow-through assay device. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF THE CASE

Claims 14-19 and 29-31 are on appeal. Claims 20-28 are also pending but have been withdrawn from consideration by the Examiner. (App. Br. 2.) We will focus on claim 14, the only independent claim on appeal, which reads as follows:

> 14. A flow-through assay device for detecting the presence or quantity of an analyte residing in a test sample, said flow-through assay device comprising a porous membrane in communication with optical detection probes conjugated with a first antibody specific for the analyte, said porous membrane defining:
>
> a competitive zone that contains a second antibody immobilized on said porous membrane that is complexed to an antigen containing an optically detectable substance prior to the application of a test sample to the device, said antigen being identical to or an analog of the analyte and said optically detectable substance being capable of producing a competitive signal when contained within said competitive zone; and
>
> a detection zone within which a third antibody is immobilized that is configured to bind to complexes formed between the analyte and said conjugated optical detection probes to produce a first detection signal, said third antibody also being configured to bind to said antigen from said competitive zone to produce a second detection signal, wherein the amount of the analyte within the test sample is determined from said competitive signal, and at least one of said first detection signal and said second detection signal.

Claims 14-16 and 29-31 stand rejected under 35 U.S.C. § 103(a) as obvious over Boehringer et al. (US 7,144,742 B2, Dec. 5, 2006) in view of Behnke et al. (US 5,573,921, Nov. 12, 1996) (Ans. 4).

Claim 17 stands rejected under 35 U.S.C. § 103(a) as obvious over Boehringer in view of Behnke and Polito et al. (US 2004/0018637 A1, Jan. 29, 2004) (Ans. 7).

Claim 18 stands rejected under 35 U.S.C. § 103(a) as obvious over Boehringer in view of Behnke and Harris et al. (US 2003/0162236 A1, Aug. 28, 2003) (Ans. 8).

Claim 19 stands rejected under 35 U.S.C. § 103(a) as obvious over Boehringer in view of Behnke and Blatt et al. (US 2005/0196875 A1, Sep. 8, 2005) (Ans. 9).

The Examiner relies on Boehringer for teaching:

> a lateral flow (flow-through) assay device for detecting the presence or quantity of an analyte residing in a test sample, said lateral flow assay device comprising a porous membrane in communication with a labeled reagent (optical detection probes) conjugated with a specific binding member, such as a first antibody, specific for the analyte, said porous membrane defining:
>
> a barrier (competitive) zone 16a that can contain either (i) a second antibody immobilized on said porous membrane that can be complexed to an antigen containing a label (optically detectable substance) during use, said antigen being identical to or an analog of the analyte and said label being capable of producing a signal; or (ii) an immobilized analyte analog; and
>
> a detection zone 16b and 16c within which a third antibody is immobilized that is configured to bind to complexes formed between the analyte and said conjugated labeled reagent to produce a first detection signal, said third antibody can also be configured to bind to said antigen or analyte analog from said barrier zone to produce a second detection signal, wherein the amount of analyte within the test sample is determined from said detection signals.

(Ans. 4.) The Examiner refers to the embodiment in which "the barrier zone comprises an immobilized analyte analog" as "a secondary or sandwich

format" and indicates that it "is the closest comparable embodiment to Appellant[s'] independent claim 14" (*id.* at 13-14).

The Examiner relies on Behnke for teaching "a test strip device for determining the amount of analyte in a sample using immunochemical displacement" (*id.* at 5). The Examiner finds:

> The test strip device contains at least one immobilized antibody, wherein the antibody is bound to an analyte analog (tracer) prior to application of test sample to the device. The bound analyte analog (tracer) can also include an attached dye (molecule or particle), such that the area of the test strip comprising the immobilized antibody and tracer can be directly visualized even before beginning the test.

(*Id.*)

The Examiner concludes that it would have been obvious

> to include with the device of Boehringer et al. the binding of the antigen or analyte analog containing an optically detectable substance to an immobilized antibody in the barrier zone prior to application of the test sample as taught by Behnke . . . because the bound analyte analog attached to the dye allows for directly visualizing the area of the test strip comprising the immobilized antibody (i.e. barrier zone) even before beginning the test, and also allows for utilizing the reduction in the dye from the area of immobilized antibody after applying the test sample in determining the amount of analyte in the sample.

(*Id.* at 5-6.)

The Examiner relies on Polito, Harris, and Blatt for teaching features of dependent claims 17-19 (*id.* at 7-10).

Appellants contend that the proposed combination fails to teach all of the limitations of claim 14, it would not have been obvious to combine the

references in the manner suggested, and the modification is based on impermissible hindsight analysis (App. Br. 8-11).

ISSUE

Has the Examiner set forth a prima facie case that Boehringer and Behnke suggest an assay device for detecting an analyte comprising: (a) a porous membrane in communication with optical detection probes conjugated with a first antibody specific for the analyte and (b) a second antibody immobilized on the porous membrane that is complexed to an antigen containing an optically detectable substance prior to the application of a test sample to the device?

FINDINGS OF FACT

1. Boehringer discloses "a method of determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member)," comprising "providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones" (Boehringer, col. 3, ll. 11-16).

2. Boehringer also discloses that the "labeling zone comprises a diffusively bound labeled first sbp member that is complementary to or analogous to the analyte" (*id.* at col. 3, ll. 17-19).

3. In addition, Boehringer discloses "a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, a barrier zone and one or more serially oriented capture zones" (*id.* at col. 3, ll. 35-39).

4. Boehringer also discloses that the "barrier zone, whether a labelled analyte analog, or a labelled sbp member complementary to the analyte, serves as a means of preventing a labelled species from migrating further along the matrix unless the analyte concentration exceeds a certain threshold level" (*id.* at col. 10, ll. 55-60).

5. In one embodiment, Boehringer discloses:

> the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, the barrier zone comprises a second sbp member analogous to the analyte immobilized in the barrier zone, and each of the one or more capture zones comprises at least a third sbp member immobilized in the one or more capture zones.

(*Id.* at col. 3, ll. 38-45.)

6. To use this embodiment, Boehringer discloses:

> [A]nalyte in the sample is first allowed to bind to labelled sbp member complementary to the analyte to form an analyte-labelled sbp member complex. The amount of unbound labelled sbp member remaining is inversely proportional to the amount of analyte in the sample. . . . Analyte analog on the barrier zone is able to bind free labelled sbp member. Generally, there is sufficient analyte analog on the barrier zone to bind all the labelled sbp member in the absence of analyte. Bound labelled sbp member flows through the barrier zone in the form of an analyte-labelled sbp member complex which is unable to bind to the immobilized analyte analog. The detection zone contains an immobilized sbp member that is capable of binding the analyte-labelled sbp member complex.

(*Id.* at col. 11. l. 67, to col. 12, l. 61.)

7. In another embodiment, Boehringer discloses:

> the labeling zone comprises a diffusively bound labeled first specific binding pair member that is analogous to the analyte, the barrier zone comprises a second specific binding pair

> member that is complementary to the analyte, and each of the one or more capture zones comprises at least a third specific binding pair member immobilized in the one or more capture zones, the third specific binding pair member being complementary to the analyte.

(*Id.* at col. 3, ll. 47-55.)

8. To use this embodiment, Boehringer discloses:

> Sample mixes with labelled antigen and passes first through the barrier zone. When no antigen is present in the sample, all the labelled antigen will bind to the barrier zone. The amount of antibody on the barrier zone must be sufficient to bind all the labelled antigen when antigen is not present in the sample. Usually, this zone will be masked off from view and will not be visible in the test device. If antigen is present in the sample, labelled antigen competes with sample antigen for the antibody immobilized in the barrier zone. If the sample contains antigen above a threshold level, the barrier zone antibody is unable to capture all of the labelled antigen. This level is controlled by the relative ratios of antigen and labelled antigen as well as the concentration and affinity of the barrier zone antibody.

(*Id.* at col. 11, ll. 8-22.)

9. Behnke discloses an immunological process for determining an analyte in a sample using a test strip "on which an antibody is immobilized in at least one partial area" (Behnke, col. 5, ll. 19-23).

10. In particular, Behnke discloses:

> The process includes bringing into contact a test solution containing the sample with one end of the test strip. The test solution is allowed to pass over at least one part of the test strip, including the partial area containing the antibody, by capillary migration. . . . The antibody is provided to be specific for the analyte. An analyte analog (tracer) is bound to the antibody and the affinity of the antibody for the analyte is higher than for the tracer. A dye or dye generating or dye providing system that is

> able to bind to the tracer is present and the tracer is displaceable by the analyte during the capillary migration of the test solution.

(*Id.* at col. 5, l. 61, to col. 6, l. 6.)

11. Behnke also discloses that, if "the tracer is visualized directly with an attached dye (molecule or particle), the area of the test strip containing the antibody is visible as a dyed area even before the beginning of the test" (*id.* at col. 7, ll. 15-18).

PRINCIPLES OF LAW

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citation omitted).

ANALYSIS

Boehringer discloses "a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, a barrier zone and one or more serially oriented capture zones" (Finding of Fact (FF) 3). The Examiner relies on Boehringer's labeling zone, barrier zone, and capture zone for suggesting, respectively, the first antibody, the competitive zone, and the detection zone of claim 14 (Ans. 4).

In one embodiment, Boehringer discloses that "the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte [and] the barrier zone comprises a second sbp member *analogous* to the analyte" (FF 5 (emphasis added)). Boehringer discloses that this device can be used in a process that we will refer to as the

non-competitive process (FF 6). In another embodiment, Boehringer discloses that "the labeling zone comprises a diffusively bound labeled first specific binding pair member that is *analogous* to the analyte [and] the barrier zone comprises a second specific binding pair member that is complementary to the analyte" (FF 7 (emphasis added)). Boehringer discloses that this device can be used in a competitive process (FF 8). The Examiner does not point to a teaching or suggestion in Boehringer in which both the labeling zone and the barrier zone comprise an sbp member that is complementary to the analyte.

The Examiner argues, however, that it would have been obvious to modify the device used in the non-competitive process, that is, the device including a barrier zone comprising a second sbp member analogous to the analyte, to use "an antibody to immobilize the analyte analog within the barrier zone" and to include "a label or optically detectable substance to the analyte analog within the barrier zone prior to the application of the test sample" based on the teachings in Behnke (Ans. 14-15). We do not agree.

In the non-competitive process, the purpose of the analyte analog in barrier zone is to bind free labelled sbp member from the labeling zone to keep it from migrating further along the matrix (FF 6 & 4). Given its purpose, we do not agree that it would have been obvious to immobilize the analyte analog in the barrier zone by an antibody, as described in Behnke, because Behnke teaches that the analyte analog would be displaced by the analyte (FF 10) and therefore would no longer be present in the barrier zone to keep the free labeled sbp from moving on to the capture zone.

With regard to the device used in Boehringer's competitive process, Appellants argue that "the 'probes' are conjugated with an *antigen*. In this manner, the antigen of the probes compete – but do not bind – with the analyte for binding sites at the barrier zone" (App. Br. 9). We agree. Even if we found that it would have been obvious, based on the disclosures in Behnke, to attach Boehringer's labeled first sbp member, which is analogous to the analyte, to the second sbp member, which is complementary to the analyte, in the barrier zone prior to application of the test sample, the Examiner has not explained why it would have been obvious to additionally include a labeled antibody that is specific for the analyte.

CONCLUSION

The Examiner has not set forth a prima facie case that Boehringer and Behnke suggest an assay device for detecting an analyte comprising: (a) a porous membrane in communication with optical detection probes conjugated with a first antibody specific for the analyte and (b) a second antibody immobilized on the porous membrane that is complexed to an antigen containing an optically detectable substance prior to the application of a test sample to the device. We are therefore compelled to reverse the obviousness rejections.

REVERSED

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